K051435

JAN 19 2006

eSensor® Cystic Fibrosis Carrier Detection System

510(k) Summary

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This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SDMA 1990 and CFR 807.92.

1. Submitter name, address, contact person and date prepared:

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Summary Prepared on January 5, 2006

2. Device Name:

eSensor® Cystic Fibrosis Carrier Detection System

Assay Component:

Device Proprietary/Trade Name: eSensor® Cystic Fibrosis Carrier Detection Kit

Common Name: CFCD Kit

Instrument Component:

Device Proprietary/Trade Name: eSensor® 4800 Instrument

Common Name: 4800 Instrument

3. Legally Marketed Equivalent Device Name

The eSensor® Cystic Fibrosis Carrier Detection System is equivalent to the Tm Bioscience Tag-It™ Cystic Fibrosis Kit 510(k) K043011, and to the Affymetrix GeneChip® Microarray Instrumentation System 510(k) K003664.

4. Intended Use of the Device

The eSensor® Cystic Fibrosis Carrier Detection (CFCD) System is a device for the detection of carrier status for cystic fibrosis for all adult couples contemplating pregnancy, regardless of ethnicity. It is a qualitative genotyping assay that simultaneously detects mutations currently recommended by the American College of Medical Genetics and American College of Obstetricians and Gynecologists (ACMG/ACOG). The eSensor® CFCD System is not indicated for prenatal screening or to establish a diagnosis of cystic fibrosis, and is for Rx only professional use within the confines of a licensed laboratory, as defined by the Clinical Laboratory Improvement Amendments (CLIA) of 1988.

5. Device Description

The eSensor® Cystic Fibrosis Carrier Detection System is an *in vitro* diagnostic test for the detection and genotyping of a selected panel of 23 cystic fibrosis mutations from DNA isolated from human whole blood.

The CFCD System is a clinical multiplex genetic test system which includes reagents for polymerase chain reaction amplification, exonuclease digestion and hybridization of target DNA, instrumentation and software. The CFCD System uses electrochemical detection to determine the carrier status of patient blood specimens for the ACOG/ACMG recommended panel of 23 cystic fibrosis mutations. Sample preparation for genotyping involves converting each blood specimen into purified genomic DNA (gDNA); then using multiplex PCR amplification followed by exonuclease digestion to convert the gDNA into a set of single-stranded targets. The genotyping reaction is set up with the combination of the single-stranded targets with appropriate buffers containing allele-specific signal probes differentially labeled with electrochemical signaling molecules, called ferrocenes. This mixture is then loaded into cartridges that contain single-stranded capture probes bound to an array of electrodes, with each electrode containing capture probes specific for a single mutation. Cartridges are inserted into the eSensor® 4800 Instrument where the single-stranded targets hybridize to the complementary sequences of the capture probes and signal probes. Detection of the target/probe complexes is achieved using alternating current voltammetry that generates specific electrical signals from the hybridized signal probes. The eSensor® DNA Detection System Application Software then classifies the signals from each mutation and generates a report for each specimen that describes the carrier or non-carrier status of each of the cystic fibrosis panel mutations.

6. Performance Characteristics:

Input DNA Requirements:

Samples containing 10 ng gDNA were tested in the CFCD System. Out of the total of 96 tests, 99.0% gave complete and accurate results, with a lower one-sided 95% confidence bound of 95.1%. Samples containing up to 1,200 ng DNA were tested in method comparison studies and gave accurate results in the CFCD System as compared to DNA sequencing.

Method Comparison:

Per sample: In Clinical Trial Method Comparison studies, 486 samples of freshly collected and banked samples were analyzed using the CFCD System and DNA sequencing. The overall agreement of the CFCD System compared to sequencing was 98.8% (479/486). Omitting samples which failed to give a valid call, agreement between the CFCD System and DNA sequencing was 99.6% (479/481).

Per mutation: Using the same data compiled for the per sample calculation above, 11,178 (486 x 23) individual mutations were analyzed. The overall agreement of the CFCD System compared to DNA sequencing was 99.0% (11,061/11,178). Omitting samples which failed to give a valid result, agreement between the CFCD System and DNA sequencing was 99.98% (11,061/11,063)..

Interfering Substances:

The following interfering substances were added separately to whole blood at the concentrations indicated, and no effect was observed on yield of extracted DNA, multiplex amplification of CFTR gene sequences, or genotyping of mutations in the CF carrier panel: triglycerides (3,000 mg/dL), high-density lipoprotein (70 mg/dL), cholesterol (250 mg/dL), bile salts (a mixture of cholate and deoxycholate; 6.4 µg/mL), human albumin (3 g/dL), human immunoglobulin G (3 g/dL), acetaminophen (30 µg/mL), ascorbic acid (30 µg/mL), diphenylhydantoin (phenytoin; 20 µg/mL), gentamicin (12 µg/mL), N-acetylsalicylic acid (200 µg/mL), nicotine (100 µg/mL), theophylline (20 µg/mL), valproic acid (100 µg/mL), vancomycin (100 µg/mL), NaCl (150 mM), KCl (5 mM), $CaCl_2$ (1.08 mM), $FeCl_3$ (9.25 µM).

Interfering Mutations:

ΔF508 reflex tests: DNA samples containing the non-disease causing polymorphisms I506V, I507V, and F508C, recommended for testing by the ACMG and ACOG in the event of unexpected homozygosity of ΔF508, have been tested internally with the CFCD System and found to genotype as non-carriers for both ΔF508 and ΔI507. The presence of the F508C polymorphism and the ΔF508 mutation in the same sample did not affect the identification of this sample as a ΔF508 carrier.

Samples heterozygous for the non-panel mutation 2183AA>G are genotyped as carriers for the panel mutation 2184delA. Samples heterozygous for the non-panel mutation R117L will give a "no-call" result for panel mutation R117H.

Reproducibility:

Reproducibility of the CFCD System was determined by testing genomic DNA samples from one non-carrier cell line and 20 carrier cell lines which together expressed all 23 panel mutations. Testing was performed at three sites with three lots of CFCD Assay Kits. Each panel of 21 cell line DNA samples was tested on separate days (5 days per kit lot per site). After re-testing of no-call results, overall per-sample agreement was 99.8%, with a no-call rate of 0.1% and a contradictory call rate of 0.1%. Overall per-mutation agreement was 99.9%, with a no-call rate of 0.1% and a contradictory call rate of 0.004%.

System Failure:

The first-pass no-call rate observed with the CFCD System in the Clinical Trial Method Comparison study of 486 samples was 3.3%, which was reduced to 1.0% after no more than 2 repeat tests for those samples which gave no-call results.

7. Conclusions

The eSensor® Cystic Fibrosis Carrier Detection System accurately identifies a selected panel of mutations in the CFTR gene from genomic DNA isolated from human whole blood.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Clinical Micro Sensors, Inc.
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JAN 19 2006

Re: k051435
Trade/Device Name: eSensor® Cystic Fibrosis Carrier Detection System
Regulation Number: 21 CFR 866.5900
Regulation Name: CFTR (cystic fibrosis transmembrane conductance regulator) gene mutation detection system
Regulatory Class: Class II
Product Code: NUA
Dated: May 31, 2005
Received: June 1, 2005

Dear Dr. Coty:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Robert L. Becker, Jr., MD, Ph.D
Director
Division of Immunology and Hematology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K051435

Device Name: eSensor® Cystic Fibrosis Carrier Detection System

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Prescription Use X AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K051435